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SENT ELECTRONICALLY & VIA CERTIFIED MAIL

Food and Drug Administration
Docket No. 2003P-0029
Division of Dockets Management
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: **Docket No. 2003P-0029**
Use of Ozone Depleting Substances; Removal of Essential Use Designation for Albuterol in Metered-Dose Inhalers (MDIs)

To Whom It May Concern:

There are currently 3,372 Rite Aid pharmacies operating in twenty-eight (28) states and the District of Columbia and on their behalf I wish to take this opportunity to provide comments on the FDA's proposed rule to remove metered-dose inhalers (MDIs) containing the active moiety albuterol from the list of essential uses of ozone-depleting substances (ODSs). Rite Aid opposes the FDA's proposed removal of the essential use designation at this point in time and respectfully requests that the agency postpone the removal of the essential use designation as long as possible.

The FDA has tentatively concluded that two non-ODS MDIs currently on the market are satisfactory alternatives to albuterol MDIs containing ODSs called chlorofluorocarbons (CFCs), and has proposed to remove the essential use designation for albuterol MDIs. (69 FR 33602-33618 (June 16, 2004)). Rite Aid understands and recognizes the need for eventual removal of harmful ODSs from all products, including CFCs in prescription MDIs. However, at this point in time, we are concerned that consumers will not be "adequately served" under the proposed rule. The proposed removal of the essential use designation for albuterol MDIs will increase costs to consumers, governments and the overall health care system. Added costs could lead to harmful effects on individuals' health status and access to services. The potential negative impact this removal may have on the consumer should be a key factor in determining whether the removal should occur.

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To minimize these impacts, Rite Aid encourages the FDA to postpone removal of the essential use designation. This postponement will provide reasonable time for existing non-ODS MDI producers to increase production and/or for new products to enter the market, ensuring adequate supplies and production, as well as sufficient price competition to assure that these products remain available to individuals who need them. Delaying the transition to non-ODS MDIs also lessens the negative economic impact created when consumers are forced to switch from relatively low cost, generic CFC-based albuterol MDIs to more expensive non-ODS branded products. A result of delaying the transition is that economic costs are minimized, alleviating the potentially harmful follow-on effects on health status and a patients' access to pharmacy services.

FDA Conditions for Removal of Essential Use Exception May Not Be Met

The FDA previously established four (4) standards that must be met before removing the essential use exception for an ODS in a medical product. (67 FR 48370 (July 24, 2002)). First, because albuterol is an active moiety marketed in ODS products represented by two (2) or more new drug applications (NDAs), there must be at least two (2) acceptable alternatives with the same route of administration and the same indication(s), with approximately the same level of convenience of use. The second requirement is that supplies and production capacity for non-ODS products exist at levels sufficient to meet patient need. Thirdly, adequate U.S. postmarketing use data must be available for the non-ODS products. Finally, patients who medically require the ODS product should be adequately served by the non-ODS products containing that active moiety and/or other available products.

The FDA has tentatively concluded that both Proventil HFA and Ventolin HFA are two (2) acceptable alternatives for albuterol MDIs containing an ODS. We agree that these hydrofluoroalkane (HFA) containing products have the same route of administration, same indication(s), and offer about the same convenience as CFC-based albuterol MDIs. Existing postmarketing data for the alternative products is also sufficient. However, we are concerned that patients may not be adequately served based upon the fact that appropriate supplies and production capacity may not exist.

FDA Should be Certain that Sufficient Production Capacity and Supplies will Exist to Meet Patient Needs

The FDA admits that it has a "relatively minimal amount of information on production capacity" and "tentatively [concludes] that capacity to produce adequate supplies of non-ODS albuterol MDIs could be in place no sooner than 12 months after date of publication... of any final rule based on this proposed rule." (69 FR 33606 (June 16, 2002)). Twelve (12) months is not sufficient time for manufacturers of the two (2) current non-ODS MDIs to increase production to adequate levels or for other manufacturers to bring lower cost products to market. We believe that manufacturers are unlikely to commit significant resources to production of non-ODS MDIs without a fixed transition date. Rite Aid recommends that the FDA establish a fixed transition date that is no less than the maximum number of months that current manufacturers indicate

will be required to produce sufficient quantities. Based on documents and discussion from the June 10, 2004, meeting of the FDA Pulmonary-Allergy Drugs Advisory Committee, both Schering-Plough and GlaxoSmithKline appear to prefer eighteen (18) months of lead time. Other statements from the same meeting suggest that the FDA does not plan to publish a final rule until early- to mid-2005. Therefore, the earliest realistic transition date is late 2006.

The FDA may consider a shorter time frame if new products are approved prior to the transition (e.g., those for which IVAX and Sepracor have submitted NDAs). New products should not be factored into the "availability equation" by the FDA until the agency approves of these new products.

Regardless of the date selected for this transition, the FDA must work closely with industry, pharmacy and advocacy groups in order to ensure that the albuterol supply—both CFC-based and non-ODS—remains adequate. It is not possible for drug manufacturers to instantly produce and distribute millions of non-ODS MDIs. Therefore, a transition period will include an increase in non-ODS production and a decrease in production of albuterol MDIs containing CFCs. If the FDA has any concern regarding the production capacity and/or supply of both new products and existing MDIs, extra time should be provided by the agency to ensure that adequate supplies will be available both during and after the transition period.

Higher Prices for Non-ODS Products will Increase Costs, Cause Harm

The removal of the essential use designation for ODS propellants will result in the replacing of lower cost generic albuterol MDIs with newer, more expensive, branded products. Retail pharmacy data for 2003 indicate that roughly 30.6 out of 32.8 million prescriptions for albuterol MDIs—roughly 93 percent—were for CFC-based generic albuterol MDIs. During this same time period there existed only 1.6 million prescriptions for Proventil HFA, 150,000 prescriptions for Ventolin HFA and approximately 400,000 prescriptions for branded albuterol products using CFC propellants.

Switching users from generic albuterol MDIs to branded non-ODS MDIs will increase costs. The retail pharmacy data cited above indicates that the average retail price of a generic albuterol MDI was $21.89 in 2003. The average retail price for the two HFA-based products (Proventil HFA and Ventolin HFA) was $46.74, more than double the price of the generics but slightly lower than the average price for brand products using CFC propellants ($52.45). It is highly unlikely that these prices will drop with the elimination of generic competition or the entry of additional branded products into the market.

Assuming the same average retail prices indicated above, switching albuterol MDIs using CFCs (both brand and generic) to HFA products would have increased spending on these prescriptions by $757.9 million in 2003. Consumers, governments and other third parties such as hospitals and health plans would bear this additional cost. For example, data for 2003 indicates that Medicaid programs in forty-six (46) states and the District of Columbia would have paid approximately $73 to $91 million more for albuterol

if they were required to pay for Ventolin HFA or Proventil HFA instead of generic MDIs. This increase exists even after accounting for the higher rebates on the branded drugs. By the FDA's estimates, the present value of the additional cost of albuterol could be $6.9 to $7.9 billion if the transition occurs as early as 2006.

Patents for Proventil HFA and Ventolin HFA begin to expire in 2010, with the last expiring in 2015. Re-entry of generic products will be delayed until these patents expire or a successful patent challenge occurs. IVAX Corporation has received an approvable letter for its albuterol sulfate HFA product. Although additional brand products will help to ensure adequate production capacity and supplies and might result in lower prices relative to a market with just two products, albuterol prices seem destined to be higher without generic competition. The availability of generic HFA products - expected to reach consumers within the next decade - will likely result in the reduction of albuterol MDI prices thereby making the transition away from ODSs more affordable to consumers, government entities and health care providers at later dates.

Removal of albuterol essential- use status poses a threat to patient access and quality patient care.

Albuterol is a life saving therapy for asthma and Chronic Obstructive Pulmonary Disease (COPD) sufferers. The transition from CFC to HFA products will undoubtedly result in price increases for albuterol MDIs. While the implications of such price increases on the overall healthcare system, patient safety, and accessibility remain unclear, a premature transition could potentially result in little benefit to consumers. Additionally, a premature transition could compromise patient care by increasing the product cost while decreasing patient compliance.

Asthma is a growing health epidemic in the United States, particularly among poor and minority populations. Many of these individuals are low income or uninsured. This population is certainly not equipped to adapt to large increases in medication costs. Price increases force patients to make decisions concerning the importance of their medications, weighing the cost of the drug versus their perceived benefits.

A study in the May 19 issue of the Journal of the American Medical Association showed antiasthmatic medications exhibit significant price responsiveness when co-payments are doubled. Use of these medications dropped approximately 30% in response to increased co-payments, demonstrating that even individuals with prescription drug insurance may respond undesirably to increased albuterol MDI prices. It is certainly not in the best interest of the FDA, community pharmacy, or the healthcare system for patients to discontinue or fail to purchase life saving rescue therapies due to the increase in the cost of the prescription drug product.

The removal of albuterol essential-use status poses a threat to the current healthcare system

The cost to the health care system of premature removal of CFCs in albuterol MDIs could potentially be much larger and more devastating than expected if the impact of a

price increase on consumers and the healthcare system is not fully considered by the FDA. Inaccessibility to medication therapy undoubtedly leads to non-compliance. The American Journal of Health- System Pharmacy in July 2003 claimed that non-compliance with prescription medications accounts for over $8.5 billion annually in increased hospital admissions and physician visits. Non-compliant asthma and COPD sufferers could realistically add millions of dollars to the nation's health-care bill, as greater morbidity, increased hospital admissions, and a heightened risk of early death are all potential consequences of denied access to albuterol because the only alternative is more expensive albuterol MDIs.

We believe the potential consequences of premature transition could also result in patients purchasing prescription medication from foreign counties or through rogue internet pharmacies. Patients are turning top these illegal sources of prescription medication in record numbers. The FDA should attempt to make the transition from CFC to HFA albuterol MDI products as affordable as possible in order to keep patients within our borders, away from dangerous counterfeit products, and at our pharmacy counters where they can receive the proper instruction and counseling necessary for such complex treatment devices.

Conclusion and Recommendations

We believe the FDA must ensure all patients will be "adequately served" by the transition before a final determination on the essential-use status of albuterol can be made. Implementation of this program at the present time could result in little benefit to consumers and may, in fact, compromise patient care. Appropriate and affordable access to this life saving therapy should be fundamental to the consideration of a final rule.

We appreciate your consideration of our views.

Sincerely,

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